

WE CLAIM:

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1. A purified cartilage extract that stimulates local cartilage formation when combined with a matrix and implanted into a mammal, said extract being produced by a method comprising:
- 5 (a) obtaining cartilage tissue;
- (b) homogenizing said cartilage tissue in the presence of chaotropic agents under conditions that permit separation of proteins from proteoglycans;
- (c) separating said proteins from said proteoglycans; and
- (d) obtaining said proteins.
- 10 2. The extract of Claim 1, wherein said extract is obtained by a method in which step (c) comprises use of a sepharose column.
3. The extract of Claim 1, wherein said extract is obtained by a method which additionally comprises the steps of separating said proteins on a molecular sieve and obtaining those proteins having a molecular weight between 30 kDa and 60 kDa.
- 15 4. The extract of Claim 1, wherein said extract is an extract of articular cartilage.
5. The extract of Claim 1, wherein said extract is an extract of epiphyseal cartilage.
6. A method of preparing a partially purified articular cartilage extract having chondrogenic activity, comprising the steps:
- 20 (a) obtaining cartilage tissue; *B*
- (b) homogenizing said cartilage tissue in the presence of chaotropic agents under conditions that permit separation of proteins from proteoglycans;
- (c) separating said proteins from said proteoglycans; and
- (d) obtaining said proteins.
- 25 7. The method of Claim 6, wherein step (c) comprises use of a sepharose column.
8. The method of Claim 7, wherein step (c) comprises isolating the proteins that bind heparin Sepharose in the presence of 0.15 M NaCl but not in the presence of 1 M NaCl.
9. The method of Claim 6, additionally comprising the steps of separating said proteins on a molecular sieve and obtaining those proteins having a molecular weight between 30 kDa and 60 kDa.
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- 30 10. An isolated DNA molecule encoding a protein having chondrogenic activity *in vivo* but substantially no osteogenic activity *in vivo*, said molecule having a nucleotide sequence that can hybridize to a polynucleotide having a nucleotide sequence selected from the group consisting of SEQ ID NO:11 and SEQ ID NO:12 at 55°C with 0.4× SSC and 0.1% SDS.
11. The isolated DNA molecule of Claim 10, wherein said molecule has a nucleotide sequence selected from the group consisting of SEQ ID NO:13 and SEQ ID NO:14.

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✓ 12. A recombinant protein having chondrogenic activity *in vivo* but substantially no osteogenic activity *in vivo*, wherein said protein has an amino acid sequence selected from the group consisting of SEQ ID NO:13 and SEQ ID NO:14.

✓ 13. A method of stimulating cartilage formation in a mammal, comprising the steps:

- 5 a) supplying cartilage-derived morphogenetic proteins having *in vivo* chondrogenic activity;
- b) mixing said partially purified proteins with a matrix to produce a product that facilitates administration of said partially purified proteins; and
- 10 c) implanting the product of step (b) into the body of mammal to stimulate cartilage formation at the site of implantation.

14. The method of Claim 13, wherein said partially purified cartilage-derived morphogenetic proteins are obtained from articular cartilage or epiphyseal cartilage.

15. The method of Claim 13, wherein the matrix of step (b) comprises a cellular material.

16. The method of Claim 13, wherein mixing step (b) additionally comprises mixing of viable chondroblast or chondrocytes.

17. The method of Claim 5, wherein the implanting step comprises implanting subcutaneously. **B**

18. The method of Claim 5, wherein the implanting step comprises implanting subcutaneously.

19. The method of Claim 5, wherein the implanting step comprises implanting intramuscularly.

✓ 20. A composition that can be administered to a mammal for the purpose of stimulating chondrogenic activity at the site of administration without substantially stimulating osteogenic activity, said composition comprising at least one cartilage-derived morphogenetic protein and a matrix.

21. The composition of Claim 20, wherein said cartilage-derived morphogenetic protein is derived from an extract of cartilage tissue.

22. The composition of Claim 20, wherein said cartilage tissue is selected from the group consisting of articular cartilage and epiphyseal cartilage.

23. The composition of Claim 20, wherein said cartilage-derived morphogenetic protein is a recombinant protein.

24. The composition of Claim 20, wherein said recombinant protein has a sequence selected from the group consisting of SEQ ID NO:13 and SEQ ID NO:14.

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25. The composition of Claim 20, wherein said matrix is selected from the group consisting of fibrin glue, freeze-dried cartilage, collagens and guanidinium-insoluble collagenous residue of demineralized bone ~~or B~~

5 26. The composition of Claim 20, wherein said matrix is a non-resorbable matrix selected from the group comprising tetracalcium phosphate and hydroxyapatite.

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